(19) World Intellectual Property Organization International Bureau



(43) International Publication Date 7 July 2005 (07.07.2005)

PCT

(10) International Publication Number WO 2005/061527 A1

(51) International Patent Classification⁷: A61P 35/00, A61K 31/70

C07H 23/00,

(21) International Application Number:

PCT/EP2004/053628

(22) International Filing Date:

21 December 2004 (21.12.2004)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 03405913.9

22 December 2003 (22.12.2003) EP

(71) Applicants (for all designated States except US): SOL-IDAGO AG [CH/CH]; Marienstrasse 18, CH-3005 Bern (CH). UNIVERSITAET ZUERICH [CH/CH]; Prorektorat Forschung, Rämistrasse 71, 8006 Zürich (CH). PAUL SCHERRER INSTITUT [CH/CH]; Center for Radiopharmaceutical Science, 5232 Villigen PSI (CH).

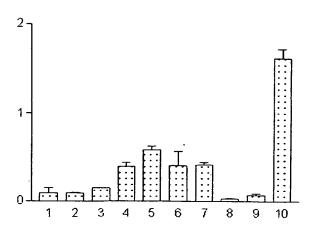
(72) Inventors; and

(75) Inventors/Applicants (for US only): TREICHLER, Hans-Jörg [CH/CH]; Ringgackerstrasse 1, CH-4447 Känerkinden (CH). ALBERTO, Roger [CH/CH]; St. Georgenstrasse 54, CH-8400 Winterthur (CH). WAIBEL, Robert [CH/CH]; Räterschenstrasse 5, CH-8352 Ricketwil (CH). KUEENZI, Martin, T. [CH/CH]; Hüslimattstrasse 48, CH-4132 Muttenz (CH). NUEESCH, Jakob [CH/CH]; Waldstrasse 14, CH-4144 Arlesheim (CH). MUND-WILER, Stefan [CH/CH]; Golattenmattgasse 9, CH-5000 Aarau (CH). VAN STAVEREN, Dave, R. [NL/NL]; Zwaardleliestraat 54, NL-3053 VX Rotterdam (NL).

- (74) Agent: BECKER, Konrad; Aeschenvorstadt 24, P.O.Box 318, CH-4010 Basel (CH).
- (81) Designated States (unless otherwise indicated. for every kind of national protection available): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH,

[Continued on next page]

(54) Title: COBALAMINE DERIVATIVES USEFUL FOR DIAGNOSIS AND TREATMENT OF ABNORMAL CELLULAR PROLIFERATION



(57) Abstract: The invention relates to cobalamin derivatives (a) having no binding affinity or low binding affinity to the transport protein transcobalamin II TCII) and (b) retaining activity as a vitamin B12 substitute, optionally carrying a therapeutic and/or diagnostic agent, such as a radioactive metal. These compounds have a much reduced accumulation rate in blood and benign organs, such as kidney and liver, compared to the accumulation rate in neoplastic tissues, and are more rapidly eliminated from blood. The invention further relates to a method of diagnosis and a method of treatment of a neoplastic disease or an infection by microorganisms in a mammal comprising (a) exposing the mammal to a period of a vitamin B12 - free diet, and (b) subsequently applying a cobalamin derivative of the invention carrying a diagnostic and/or therapeutic agent. By selecting cobalamin derivatives acting as vitamin B12 substitutes, the risk of the formation of resistant offspring in neoplastic tissue is much reduced.

WO 2005/061527 A1

GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.